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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/927,779	08/09/2001	Michael L. Roukes	049411-0204	5454

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EXAMINER	
LAM, ANN Y	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 02/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/927,779	ROUKES ET AL.	
	Examiner	Art Unit	
	Ann Y. Lam	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,11-26,34-37,40,42,43,46,47,49,50 and 53* is/are pending in the application.

4a) Of the above claim(s) *6-10,33,38,39,41,44,45,48,51,52 and 54-60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,11-26,34-37,40,42,43,46,47,49,50 and 53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of group II in the reply filed on October 21, 2005 is acknowledged. The traversal is on the ground(s) that claims 2-4, 11-26 and 34-36 should be examined with the elected claims of group II because elected claim 5 does not recite characteristics which are mutually exclusive from claims 2-4, 11-26 and 34-36. Applicant's arguments are persuasive and claims 2-4, 11-26 and 34-36 are considered along with group II, as set forth below.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-5, 11-26, 34-37, 40, 42, 43, 46, 47, 49, 50 and 53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 37, 47 and 53 recite in the preamble "a detector.....comprising". The body of the claim however, recites a detector among other things, such as a reservoir, and a resonator, and/or a substrate. It is not clear as to what comprises the detector. (Does it include the reservoir and resonator and substrate?)

Claim 5, line 3, recites a ligand capable of molecular interaction with the receptor. It is not clear as to whether the ligand in claim 5 is the "molecules" being detected in the preamble in claim 1, line 2.

Independent claims 1, 37, 47, and 53 each recite that the resonator is "nanometer-scale". However, the specification describes a range that includes dimensions that are not in the nanometer scale but are in the micron scale (see page 4, lines 14-15). Also, dependent claim 17 recites dimensions that are in the micron scale also. It is not clear as to what Applicant means by "nanometer-scale". (Does it include resonators that have one or more dimensions that are in the micron scale? Does it encompass resonators that have all dimensions in the micron scale?)

Claim 37 recites "a substrate or a second resonator". Does it mean that the substrate is a second resonator? (For purposes of examination, claim 37 and dependent claim 43 are interpreted to mean that the substrate is considered a second resonator.)

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

3. Claims 1, 2, 4, 5, 11, 12, 15, 23, 25, 26, 34, 37, 40, 42, 43, 46, 47, 50 and 53 are rejected under 35 U.S.C. 102(e) as being anticipated by Weitekamp, 6,911,646.

As to claims 1, 34, 53, Weitekamp discloses a molecular detector capable of detecting single-molecules in solution comprising;

a solution reservoir (112, see col. 4, line 25);

at least one biofunctionalized nanometer-scale mechanical resonator disposed within the reservoir ("oscillator, col. 4, line 26, and col. 11, line 16); and

a detector in signal communication with the at least one resonator for measuring a damping of resonance motion of the resonator in response to a molecular binding event on the resonator (col. 11, lines 16-22).

As to claim 2, the at least one resonator comprises a vibrational resonator (col. 11, lines 16-21).

As to claim 4, the at least one resonator is biofunctionalized with a receptor (110, see col. 4, lines 24-25).

As to claims 5, 42, 43 and 47, the device further comprises a substrate ("surface", on col. 4, line 25) disposed within the reservoir and adjacent to the at least one resonator, wherein the substrate is biofunctionalized with a ligand capable of molecular interaction with the receptor (col. 4, lines 24-33).

As to claim 11, the at least one resonator is made from silicon (col. 20, lines 51-55).

As to claim 12, the detector is integral with the resonator (see fig. 3).

As to claim 15, the detector is an optical detector (col. 11, lines 16-18).

As to claims 23, the resonator is biofunctionalized to detect a receptor/ligand interaction (col. 4, lines 24-33).

As to claim 25, the resonator is biofunctionalized to detect a chemical bond (col. 4, lines 25-28).

As to claim 26, the resonator is biofunctionalized to detect protein unfolding (col. 4, lines 25-28). (Because Applicant is claiming an apparatus, the prior art meets the claim if it is capable of performing the claimed intended use. In this case, the resonator is capable of detecting protein unfolding.)

As to claim 37, the detector measures a mechanical displacement of the resonator (col. 11, lines 16-21).

As to claims 40 and 50, the substrate ("surface", on col. 4, line 25) is disposed in the reservoir (112).

As to claim 46, a driving element as claimed is disclosed (see oscillator, col. 6, line 49.)

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 17-22, 35, are rejected under 35 U.S.C. 103(a) as being unpatentable over Weitekamp, 6,911,646.

Weitekamp teaches the invention substantially as claimed (see above).

As to claim 17 and 35, however, Weitekamp does not teach that the resonator has the dimensions specifically as claimed by Applicant.

Weitekamp however teaches that the resonator is in the nanoscale range and that sensitivity improves as the resonator is reduced in size (col. 11, lines 16-22).

Moreover, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233. In this case, Weitekamp teaches the invention substantially as claimed, and discovering the optimum or workable ranges of the dimensions in the nanometer (and micron) scale as recited in claim 17, involves only routine skill in the art.

Also, as to claims 18-22, Weitekamp does not disclose that the resonator has a resonance motion vacuum frequency between about 0.1 and 12 MHz (claim 18), nor a force constant between about 0.1mN/m and 1N/m (claim 19), nor a Reynolds number between about 0.001 and 2.0 (claim 20), nor a mass loading coefficient between about 0.3 and 11 (claim 21), nor a force sensitivity of about 8fN/$\sqrt{Hz}$ or greater (claim 22).

However, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233. In this case, Weitekamp discloses the general conditions of the claims (see above with respect to claim 1), and the ranges recited in claims 18 through 22 relate to optimum or workable ranges and thus involve only routine skill in the art according to *In re Aller.*

5. Claims 3, 13, 16, 36, 49, are rejected under 35 U.S.C. 103(a) as being unpatentable over Weitekamp, 6,911,646, in view of Thundat, 6,289,717.

Weitekamp teaches the invention substantially as claimed (see above).

As to claim 3, Weitekamp does not teach that the cantilever has a plurality of spring elements. However, Thundat teaches a cantilever having a plurality of spring elements (col. 3, lines 66-67). (This embodiment is disclosed in figure 2 and is a notched cantilever.)

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize a notched cantilever taught by Thundat et al. as the Weitekamp cantilever because Thundat et al. teaches that cantilevers with multiple spring elements (i.e., notched cantilevers) are known in the art and provide the advantage of detecting binding to probes on the spring elements.

As to claims 13, 36 and 49, Weitekamp does not teach that the detector is a piezoresistive transducer or piezoresistive detector layer on the resonator. (Weitekamp teaches use of an optical detector, but does not teach use of a piezoresistive transducer as the detector.)

Thundat however teaches that a piezoelectric detector is an alternative detection means to an optical detector (col. 5, lines 1-23). Thundat teaches that the piezoresistive detection means is conventionally known (col. 5, lines 16-20). It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize a piezoresistive transducer or layer on the resonator as the detector in the

Weitekamp invention because Thundat teaches that the piezoresistive detector is a functional equivalent to the optical detector and are conventional in the art.

As to claim 16, Weitekamp does not teach that the detector is a lock-in detector. However, Thundat teaches that the detector may be a lock-in detector (i.e., a piezoresistive transducer, col. 5, line 17.) (Applicant's disclosure of a lock-in detection scheme is on page 20 of the specification. The detector disclosed by Thundat et al. is capable of performing this function.) It would have been obvious to one of ordinary skill in the art to utilize a piezoresistive transducer or a lock-in detector as taught by Thundat as the detector in Weitekamp because Thundat teaches that these detectors are known alternatives to optical detectors such as the one disclosed by Weitekamp.

6. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Weitekamp, 6,911,646, in view of Thundat, 6,289,717, as applied to claim 13, and further in view of Chui et al., "Independent detection of vertical and lateral forces with a sidewall-implanted dual-axis piezoresistive cantilever", Applied Physics Letters, Vol. 72, Number 11, March 1998, pp. 1388-1390.

Weitekamp in view of Thundat teaches the invention substantially as claimed (see above with respect to claim 13), except for the transducer being made of p+ doped silicon.

Chui et al. teach that a piezoresistive sensor that is p doped provides high conductivity for detection of forces (see page. 1388, right column). It would have been

obvious to one of ordinary skill in the art at the time the invention was made to provide a p doped piezoresistive sensor as taught by Chui et al. in the Weitekamp-Thundat invention because Chui et al. teach that a piezoresistive sensor that is p doped provides the advantage of high conductivity for detection of forces.

7. Claim 24 is rejected under 35 U.S.C. 102(b) as being anticipated by Weitekamp, 6,911,646, in view of Fritz et al., ("Translating Biomolecular Recognition into Nanomechanics", Science, 14 April 2000, pages 316-319, Vol. 288.)

Weitekamp discloses the invention substantially as claimed (see above), except for the resonator being biofunctionalized to detect DNA hybridization.

Fritz et al. discloses a cantilever biofunctionalized with DNA for detecting hybridization and thus DNA sequences or single base mismatch (see for example page 317, first column and abstract).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to biofunctionalize the Weitekamp cantilever with DNA as taught by Fritz et al. because Fritz et al. teaches that such biofunctionalization provides the advantage of detecting single base mismatch.

8. Claims 1-4, 11-13, 15-17, 23, 25, 26, 34, 35, 36, 53, are rejected under 35 U.S.C. 103(a) as being unpatentable over Czaplewski, "Mechanical resonant immunospecific biological detector", Applied Physics Letters, Vol. 77, No. 3, pp. 450-452, in view of Thundat, 6,289,717.

Czaplewski teaches the invention substantially as claimed.

More specifically, as to claims 1 34 and 53, Czaplewski discloses a molecular detector capable of detecting single-molecules in solution comprising;

a solution reservoir (page 451, left column, last full paragraph, disclosing a solution of cells)

at least one biofunctionalized mechanical resonator disposed within the reservoir (page 451, left column, last full paragraph, disclosing a cantilever with immobilized antibodies, and immersing the cantilever in a solution with E. coli cells, and page 452, first paragraph); and

a detector in signal communication with the at least one resonator for measuring a damping of resonance motion of the resonator in response to a molecular binding event on the resonator (page 451, left column, last paragraph, disclosing detection of a shift in the resonant frequency based on the mass loading caused by binding of cells to antibodies).

However, Czaplewski does not teach that the resonator is nanometer-scale. (Czaplewski only gives examples of the resonator being in the micron size, see page 451, left column, first full paragraph).

However, Thundat teaches resonators in a preferred embodiment that have dimensions that range from nanometers to microns (col. 3, lines 55-57). It would have been obvious to one of ordinary skill in the art at the time the invention was made to form the resonator in the Czaplewski invention in the nanometer-scale as taught by Thundat because Thundat teaches the dimensions in the nanometer-scale as a preferred embodiment. (Also, the Office notes that although Applicant claims "nanometer-scale" resonator, the dimensions disclosed in the specification includes dimensions that are not all in the nanometer-scale, such as the length, which is disclosed as being between about 1 micron to 10 micron, see page 4, lines 15-16.)

As to claim 3, Czaplewski also does not teach that the cantilever is a notched cantilever. However, Thundat teaches that the cantilever may have a plurality of spring elements (col. 3, lines 66-67). This embodiment is disclosed in figure 2 and is a notched cantilever. It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize a notched cantilever taught by Thundat et al. as the Czaplewski cantilever because Thundat et al. teaches that cantilevers with multiple spring elements (i.e., notched cantilevers) are known in the art and provide the advantage of detecting binding to probes on the spring elements.

As to claims 13 and 36, Czaplewski also does not teach that the detector is a piezoresistive transducer. However, Thundat teaches that the detector may be a piezoresistive transducer, as an alternative to other types of detectors such as laser optical detectors (col. 5, lines 4-19.) It would have been obvious to one of ordinary skill in the art to utilize a piezoresistive transducer as taught by Thundat as the detector in

Czaplewski because Thundat teaches that it is a known alternative to optical detectors such as the one disclosed by Czaplewski.

Also, as to claim 16, Czaplewski does not teach that the detector is a lock-in detector. However, Thundat teaches that the detector may also be a lock-in detector (i.e., a piezoresistive transducer, col. 5, line 17.) (Applicant's disclosure of a lock-in detection scheme is on page 20 of the specification. The detector disclosed by Thundat et al. is capable of performing this function.) It would have been obvious to one of ordinary skill in the art to utilize a lock-in detector as taught by Thundat as the detector in Czaplewski because Thundat teaches that it is a known alternative to optical detectors such as the one disclosed by Czaplewski.

As to claim 17 and 35, Czaplewski also does not teach the dimensions as claimed by Applicant. However, Thundat discloses that the cantilevers are in the nanoscale. Thundat discloses that in a preferred embodiment the resonator has a thickness between about 10 nm and 1 um (col. 3, line 57), a width between about 10 nm and 1um (col. 3, line 57), and a length between about 1 um and 10 um (col. 3, line 56.)

It would have been obvious to one of ordinary skill in the art at the time the invention was made to produce the Czaplewski cantilevers in the nanoscale dimensions taught by Thundat because Thundat teaches that these dimensions are preferred. Moreover, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233.

As to the following claims, Czaplewski teaches the limitations as follows.

As to claim 2, the at least one resonator comprises a vibrational resonator (page 451, cantilever).

As to claim 4, the at least one resonator is biofunctionalized with a receptor (page 451, left column, last paragraph).

As to claim 11, the at least one resonator is made from silicon (page 450, second paragraph, second sentence).

As to claim 12, the detector is integral with the resonator (see Fig. 1, and page 452, first paragraph).

As to claim 15, the detector is an optical detector (page 450, Figure 1).

As to claims 23, the resonator is biofunctionalized to detect a receptor/ligand interaction (page 452, first paragraph).

As to claim 25, the resonator is biofunctionalized to detect a chemical bond (page 451, last paragraph).

As to claim 26, the resonator is biofunctionalized to detect protein unfolding (page 451, last paragraph). (Because Applicant is claiming an apparatus, the prior art meets the claim if it is capable of performing the claimed intended use. In this case, the resonator is capable of detecting protein unfolding.)

9. Claim 24 is rejected under 35 U.S.C. 102(b) as being anticipated by Czaplewski, ("Mechanical resonant immunospecific biological detector", Applied Physics

Letters, Vol. 77, No. 3, pp. 450-452), in view of Fritz et al., ("Translating Biomolecular Recognition into Nanomechanics", Science, 14 April 2000, pages 316-319, Vol. 288.)

Czaplewski discloses the invention substantially as claimed (see above), except for the resonator being biofunctionalized to detect DNA hybridization.

Fritz et al. discloses a cantilever biofunctionalized with DNA for detecting hybridization and thus DNA sequences or single base mismatch (see for example page 317, first column and abstract).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to biofunctionalize the Czaplewski cantilever with DNA as taught by Fritz et al. because Fritz et al. teaches that such biofunctionalization provides the advantage of detecting single base mismatch.

10. Claims 18-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Czaplewski, "Mechanical resonant immunospecific biological detector", Applied Physics Letters, Vol. 77, No. 3, pp. 450-452, in view of Thundat, 6,289,717.

Czaplewski in view of Thundat discloses the invention substantially as claimed (see above), except for the resonator having a resonance motion vacuum frequency between about 0.1 and 12 MHz (claim 18), a force constant between about 0.1mN/m and 1N/m (claim 19), a Reynolds number between about 0.001 and 2.0 (claim 20), nor a mass loading coefficient between about 0.3 and 11 (claim 21), or a force sensitivity of about 8fN/$\sqrt{}$Hz or greater (claim 22).

It has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233. In this case, Czaplewski discloses the general conditions of the claims (see above with respect to claim 1), and the ranges recited in claims 18 through 22 relate to optimum or workable ranges and thus involve only routine skill in the art according to *In re Aller.*

Conclusion

Rourkes, "Nanoelectromechanical Systems", Technical Digest of the 2000 Solid-State Sensor and Actuator Workshop, June 2000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ann Y. Lam whose telephone number is 571-272-0822. The examiner can normally be reached on M-Sat 11-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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01/09/06